REMARKS

Claims 6 and 8-10 are pending in the instant application. Claims 6 and 10 have been rejected. Claims 6 and 8-10 are objected to. After entry of these arguments, Claims 6 and 8-10 will remain pending.

The following arguments and evidence are responsive to the Final Official Action mailed on April 14, 2009.

Applicants would like to thank Examiner Havlin for discussing the pending application with their representative Nicole Beeler on June 22, 2009. The Examiner's guidance is appreciated.

Rejection of Claims 6 and 10 under 35 USC §103(a)

The Examiner has rejected Claims 6 and 10 under 35 U.S.C. §103(a), as allegedly being unpatentable over Joshi et al. (Journal of the Indian Chemical Society) in view of Silverman, R.B. (the Org. Chem. Of Drug Design and Drug Action, Academic Press, Inc.: San Diego, 1992, pp.4-51). Specifically, the Examiner does not believe that Applicants have met their burden in demonstrating how the unexpected result would be applicable to the entire claim scope.

Applicants respectfully traverse this rejection. Applicants do not believe that the Joshi reference is analogous art. The present invention claims novel 2,5-difulouro substituted dihydropyrazoles, which are useful in the treatment of cancer by inhibiting kinesin spindle protein. The ability to inhibit the kinsein spindle protein is affected by the particular substitution pattern on the phenyl ring.

The Joshi reference teaches substituted dihydropyrazoles that have use as antifertility agents. Presumably, the ability to prevent fertility is affected by the particular substitution pattern on the phenyl ring.

The pharmaceutical sciences are highly unpredictable, and it is difficult to predict the activity of a compound merely by looking at it. After reviewing the Joshi reference, one skilled in the art would not expect the compounds described therein to be effective for any other use that as an antifertility agent. The Joshi reference does not teach the use of dihydropyrazoles for the treatment of cancer, and as such, one skilled in the art would not be motivated to use the compounds disclosed therein for the treatment of cancer via inhibition of kinesin spindle proteins.

The compounds disclosed in Joshi do not render the instantly claimed compounds obvious. Applicants are submitting the declaration of Christopher D. Cox, PhD to support the unexpected result arguments advanced in Applicants' response of January 15, 2009.

Drug discovery and design is a complex process, and the activity of seemingly similar compounds can be vastly different when tested. Applicants maintain that the 2,5-difluoro analogs of the instant invention are not obvious in light of the Joshi reference because they are more potent inhibitors of KSP than the compound in the Joshi reference, which has a 3,4-difluoro substitution pattern. As explained in Dr. Cox's declaration, The 2,5 difluoro substitution on the 3-phenyl unexpectedly results in a favorable profile when compared to mono-fluorinated and other di-fluorinated analogues. The 2,5-difluoro compounds are very potent inhibitors of kinesin spindle protein (hereinafter "KSP"). Dr. Cox and his colleagues noted that substitution at the 3-position resulted in a moderate loss in potency when compared to substitution at the 2-position, and substitution at the 4-position resulted in a dramatic loss of potency. When examining difluoro substituted phenyls, Dr, Cox noticed, quite unexpectedly, that the 2,5-disubustitution was best (94 nM). The 3,4-difluoro compound was never made based on the lack of potency observed when a halogen was at the 4-position. However, Dr. Cox explains that he would expect the 3,4-difluoro compound to have a potency of > 10,000 nM.

In light of these arguments, Applicants respectfully request the rejections of Claims 6 and 10 under 35 USC §103(a), be withdrawn.

Objection to Claims 8 and 10

The Examiner has objected to Claims 8 and 10 as being dependent on a rejected base claim. Applicants believe that Claims 6 and 8-10 are in condition for allowance, and respectfully request that the objection to Claims 8 and 10 be withdrawn.

Prior Art Reference of Record

The Examiner has made Sangwan et al., *Chimica Acta Turcica 11 (1983)* of reference. The Sangwan reference teaches 4,5-dihydropyrazole compounds that are useful as antimicrobial agents. Applicants do not believe that Sangwan has any affect on the patentability of the instant application.

The compounds presently claimed in the instant application are novel 2,5-difulouro substituted dihydropyrazoles. Sangwan does not teach difluoro substituted dihydropyrazoles.

Also, Applicants do not believe that the Sangwan reference is analogous art. The present invention claims novel 2,5-difulouro substituted dihydropyrazoles, which are useful in the treatment of cancer by inhibiting kinesin spindle protein. The ability to inhibit the kinsein spindle protein is affected by the particular substitution pattern on the phenyl ring.

Sangwan teaches substituted dihydropyrazoles that have use as antimicrobial agents. Presumably, the ability to treat bacterial and fungal infections is affected by the particular substitution pattern on the phenyl rings. After reviewing the Sangwan reference, one skilled in the art would not expect the compounds described therein to be effective for any other use that as an antimicrobial agent. The Sangwan reference does not teach the use of dihydropyrazoles for the treatment of cancer, and as such, one skilled in the art would not be motivated to use the compounds disclosed therein for the treatment of cancer via inhibition of kinesin spindle proteins.

If a telephonic communication with the Applicants' representative will advance the prosecution of the instant application, please telephone the representative indicated below. Applicants believe no additional fees are due but the Commissioner is authorized to charge any fees required in connection with this response to Merck Deposit Account No. 13-2755.

Respectfully submitted,

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Date: June 23, 2009

Enclosures: (1) Declaration of Christopher D. Cox
(2) Exhibit 1 – Curriculum Vitae – C.D. Cox